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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,805	01/19/2005	Andrew Lennard Lewis	Q83534	5416

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EXAMINER	
PURDY, KYLE A	
ART UNIT	**PAPER NUMBER**
4173	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,805	LEWIS ET AL.	
	Examiner	Art Unit	
	Kyle A. Purdy	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 31, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 37-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 1 sheet
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election Acknowledged

1. Applicants' election with traverse of the invention of Group I encompassing claims 1-28 and 37-44 in the reply filed on August 31, 2007 is acknowledged. The traversal is on the grounds that the reference does not teach the technical feature present in Groups I and II. Specifically the special technical feature is that the copolymer comprises a hydrophilic block and hydrophobic block, and further comprises a biological active compound associated with the polymer. Applicants arguments are persuasive.

2. However, a new reference is being applied in order to break unity between Groups I and II. The common feature of an amphiphilic block copolymer and a biologically active compound cannot qualify as a special technical feature as it does not provide a contribution over the prior art because it is disclosed by Konno et al. (Biomaterials, 2001, 22, 183-1889). Konno et al. specifically teaches a nanoparticle comprising a hydrophobic and a hydrophilic block, wherein a biologically active compound is associated with the molecule. Therefore, Groups I and II lack unity as the reference specifically suggests the claimed elements.

3. Claims 1-28 and 37-44 are presented for examination on the merits. The following rejections are made.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **Claims 17-19 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.**

6. The disclosure of the instant invention is directed to an aqueous composition comprising an amphiphilic diblock copolymer (i.e. A-B) wherein the diblock copolymer contains a hydrophilic block and a hydrophobic block which is dispersed in the solution, wherein the hydrophilic block has a zwitterionic group. The diblock copolymer further comprises a biologically active molecule which is associated with the polymer through hydrophobic interactions. The compositions hydrophilic and hydrophobic blocks may include comonomers that may take the generic form A/C-B/C where the comonomer is randomly integrated into their respective blocks ('substituted diblock copolymers).

7. Although a generic chemical structure is provided for the comonomers, generic drawings or structural information alone does not provide sufficient written description for an invention as required set forth by U.S.C. 112 because nowhere in the specification is such a substituted diblock copolymer described. Moreover, Applicant has failed to reduce the invention to practice. As stated by the MPEP 2163, reduction to practice does not occur until the inventor has determined that the invention will work for its intended purpose. The intended purpose of the instant application is drug delivery but since no demonstration has been presented wherein said substituted diblock copolymers can actually have such a function, it follows that the invention

has not sufficiently been reduced to practice. Additionally, there are no specific examples, protocols for synthesis or data regarding said substituted diblock polymers containing a biologically active material. Therefore, it would require undue experimentation to determine all of the groups which are encompassed by comonomer and how to include these into the claimed compound.

8. **Claims 17-19 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthesis of diblock polymers (i.e. A-B), does not reasonably provide enablement for the synthesis of substituted diblock polymers (i.e. A/C-B/C). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.**

9. There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court *In re Wands* (8 USPQ2d 1400 (FACF 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the sate of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

10. The disclosure of the instant invention is directed to an aqueous composition comprising an amphiphilic diblock copolymer (i.e. A-B) wherein the diblock copolymer contains a hydrophilic block and a hydrophobic block which is dispersed in the solution, wherein the

hydrophilic block has a zwitterionic group. The diblock copolymer further comprises a biologically active molecule which is associated with the polymer through hydrophobic interactions. The compositions hydrophilic and hydrophobic blocks may include comonomers that may take the generic form A/C-B/C where the comonomer is randomly integrated into their respective blocks ('substituted diblock copolymers). However, Applicant provides no direction regarding formulations or synthetic protocols teaching how one is to go about synthesizing such substituted diblock copolymers. The only protocol set forth is for the synthesis of diblock copolymers, such as the copolymerization of 2-methacryloyloxyethyl phosphorylcholine with 2-(diethylamino)ethyl methacrylate (MPC-DEA) (see examples 1-17). It is not described anywhere in the specification how one is to synthesize said substituted diblock copolymers. Also, nowhere in the specification is it demonstrated that these substituted diblock copolymers are actually able to act as carriers for biologically active agents. Specific and multiple working examples are critical in cases involving complicated art and since there are no such working examples provided, the specification is not enabling.

11. Therefore, the amount of guidance necessary to make Applicants invention would result in undue experimentation because the skilled artesian would be forced to randomly test numerous conditions to determine which conditions provide for the prevention of prevention of such disclosed conditions. Hence, the amount of guidance present in the specification fails to present the necessary instruction such that one can readily determine the appropriate requirements or conditions of the instant claims.

Claim Rejections - 35 USC § 102

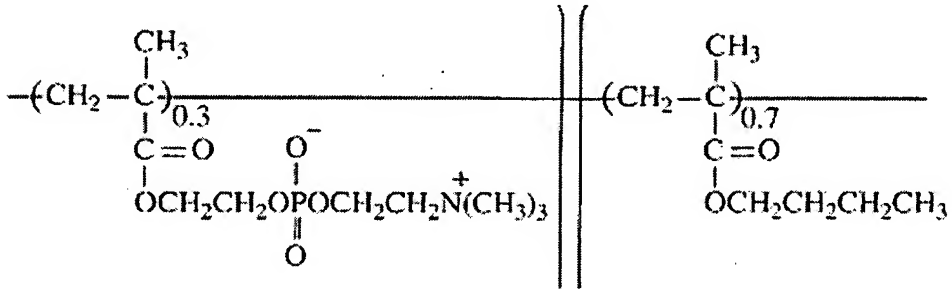
12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. **Claims 1-14, 28 and 37-38 are rejected under 35 U.S.C. 102(a) as being anticipated by Konno et al. (Biomaterials, 2001, 22, 1883-1889).**

14. The disclosure of the instant invention is directed to an aqueous composition comprising an amphiphilic diblock copolymer wherein the diblock copolymer contains a hydrophilic block and a hydrophobic block which is dispersed in the solution, wherein the hydrophilic block has a zwitterionic group. The diblock copolymer further comprises a biologically active molecule which is associated with the polymer through hydrophobic interactions.

15. Konno et al. ('Konno) is directed to the preparation of microspheres comprising bioinspired 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer. The synthesized particles possess hydrophilic and hydrophobic blocks, which are synthesized by radical polymerization (see page 1884, Experimental: 2.1). A specific example of the hydrophilic and hydrophobic monomers copolymerized are MPC and butyl methacrylate (BMA), respectively. The diblock copolymer possesses the following structure (see page 1884, right column):



These amphiphilic block copolymers are useful because they provide a convenient means for delivering drugs or fluorescent molecules. It is stated that the adsorption of drugs and other molecules to the copolymer occurs though hydrophobic interactions, which is very convenient because most fluorescent molecules and drugs have hydrophobic regions (see page 1884, left column, first paragraph). Some specific species of molecules adsorbed to the copolymer includes that of *N*-phenyl-1-naphthylamine (NPN) and bovine serum albumin (see page 1885, Experimental: 2.4 and 2.5). NPN possess an octanol:water partition coefficient of at least 1 (see physical properties section of IPCS INCHEM reference). Additionally, according to the INCHEM reference states that NPN is extremely toxic to aquatic organisms, thus NPPN is a cytotoxic compound (see Environmental Data).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. **Claims 15-16, 20-27 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konno et al. (Biomaterials, 2001, 22, 1883-1889) in view of Lobb et al. (J. AM. Chem. Soc., 2001, 123, 713-7914) further evidenced by Coessens (Prog. Polym. Sci., 2001, 26, 337-377).**

18. Konno et al. (see discussion above) fails to teach the inclusion of a hydrophobic block that contains an ionisable group. Konno also fails to teach the specific polydispersity of the

copolymer, the degree of polymerization for the hydrophilic and hydrophobic blocks, the means for polymerization of the hydrophilic block of the polymer that is specifically atom transfer radical polymerization.

19. Lobb et al. ('Lobb) teaches a composition and a mode of synthesis for biocompatible phosphorylcholine-based methacrylate copolymers via atom transfer radical polymerization (see page 7913, column one, first paragraph). Specifically, the reference of Lobb teaches the copolymerization of MPC with 2-(diethylamino)ethyl methacrylate (DEA) (see page 7914, left column, fourth paragraph) which forms micelles with a hydrophobic core comprising DEA. It is stated that the polydisperity of the MPC homopolymer is around 1.18 to about 1.45 (see page 1793, right column, third paragraph). Although Lobb is silent to the polydispersity of the hydrophobic block and the copolymer as a whole, these would most likely have polydispersity values less than 2, most likely around 1.3. This is evidenced by Coessens et al. as it stated that the method in use, atom transfer radical polymerization, creates well-defined, precisely controlled polymers with polydispersities generally lower than 1.3 (see Coessens, page 339, last paragraph). The synthesis of the MPC homopolymer as well as the MPC-DEA copolymer required the initiator oligo(ethylene glycol) bromide reaction product (OEGBr) as a catalyst for the atom radical transfer polymerization process which is a hydrophobic polymer compound and is responsible for forming the DEA and MPC homopolymers as well as the amphiphilic copolymer (see page 7914, left column, fourth paragraph). The degree of polymerization for the hydrophilic block and hydrophobic block are 30 and 100, respectively; it follows that the ratio of the degrees of polymerization for the hydrophilic and hydrophobic blocks is 10:3 or (3.33:1) (see

Fig. 2). The teaching of Lobb also includes a hydrophobic group containing an ionisable group, being that of diethylamino (see Fig. 2).

20. It would have bee obvious to one of ordinary skill in the art to combine the teachings of Konno et al. with that of Lobb et al. because in doing so would create a nanoparticle which would have the desired properties of that claimed in the instant application. For instance, it is taught by Konno that the phosphorylcholine group is useful because of its excellent blood compatibility and because it does not illicit an undesirable immunological response (see page 1883, column one, first paragraph). Further, Konno teaches a block copolymer comprising a hydrophobic and hydrophilic block wherein the hydrophilic block consisted of MPC monomers but the hydrophobic block failed to contain an ionisable hydrophobic group. However, Lobb not only teaches the homopolymierzation of MPC but also teaches the copolymerization of MPC with DEA, which comprises the hydrophobic block and also contains an ionisable group, specifically that of diethylamine. Additionally, the micelles taught by Lobb have a hydrophilic exterior comprising the phosphorylcholine group and a hydrophobic interior, the hydrophobic interior provides a thermodynamically stable environment for hydrophobic molecules such as drugs which modulates their release. Therefore, it would be obvious to one skilled in the art to combine the teaching of Konno with that of Lobb with more than a reasonable expectation of success.

21. It is noted that Coessens was cited to reinforce the fact that atom transfer radical polymerization generally results in a polydispersity of around 1.3.

Conclusion

22. The elected species are found allowable. The search was expanded and an amphiphilic copolymer comprising 2-methacryloyloxyethyl phosphorylcholine (MPC) and butyl methacrylate (BMA) was found wherein the biologically active agent *N*-phenyl-1-naphthylamine (NPN) was associated with the copolymer was found. See above rejections.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Ardin Marschel and Cecilia Tsang, can be reached on 571-272-0718 or 571-272-0562, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

25. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kyle A. Purdy
Examiner

10/4/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER